UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

VB

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/187,385	11/06/98	MARKOVIC S	07039/119001

HM12/1206

MARK S ELLINGER
FISH AND RICHARDSON
SUITE 3300
60 SOUTH SIXTH STREET
MINNEAPOLIS MN 55402

EXAMINER	
HOLLERAN, A	

ART UNIT	PAPER NUMBER
1642	5

DATE MAILED: 12/06/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/187,385	Markovic, S.N.
Examiner	**Group Art Unit**
Anne Holleran	1642

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-26* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 7, 8, and 13-26* is/are rejected.

☒ Claim(s) *2-6 and 9-12* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Priority

1. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 10-12, of this application.

Drawings

2. The drawings are objected to for the reasons indicated on the enclosed PTO-948. Correction is required.

Claim Rejections - 35 USC § 112, second paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 17-20, 24 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is vague and indefinite because it is not clear how the limitation "wherein said malignant tumor is a solid tumor" further limits the scope of claim 1 which is drawn to a method of treating a human patient having "a resectable malignant tumor".

Claims 24 and 25 are vague and indefinite because it is not clear how the claimed article of manufacture comprising an α-interferon composition is limited by the recitation that the article of manufacture include packaging material comprising a label or package insert indicating the effectiveness of administering an immunostimulatory dosage of α-interferon before surgical resection of a tumor or in conjunction with treating a tumor with non-surgical methodologies. Furthermore, it is not clear how the claims are drawn to different subject matter. Therefore, claims 24 and 25 appear to be duplicates of each other. For purposes of comparison with the prior art, claims 24 and 25 will be interpreted to be drawn to kits comprising α-interferon.

Claim Rejections - 35 USC § 112, first paragraph

5. Claims 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 13 and 14 are drawn to methods of treating a human patient having a resectable malignant tumor comprising administering an immunostimulatory dosage of an α-interferon composition wherein the immunostimulatory dosage increases B-lymphocyte activation or B-lymphocyte function. The specification defines immunostimulatory dosages in general as a dose that is about 3×10^6 U/m^2 or lower. The specification discloses that α-interferon increase natural killer cell activity. The art teaches that α-interferon increases natural killer cell activity and also cytolytic T-cell activity and function. However, the specification does not teach why one of skill

in the art would expect α-interferon to increase B-lymphocyte activity. Thus, one of skill in the art cannot determine whether the inventor had possession of the claimed invention at the time the invention was filed.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Ucar et al. (Ucar, R. et al., Annals of Allergy, Asthma, and Immunology, 75: 377-386, 1995; IDS Ref. "DI").

Claims 24 and 25 are drawn to articles of manufacture comprising α-interferon compositions. Ucar et al disclose three commercial preparations of α-interferon (page 380, 3rd column and Table 4) that is the same as that claimed.

8. Claim 26 rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 4,846,782 (published Jul. 11, 1989 to Bonnem; IDS Ref. "AA")

Claim 26 is drawn to a method for treating a human patient with a non-resectable malignant tumor, comprising administering an immunostimulatory dosage of an α-interferon

composition and treating said patient with effective non-surgical medical methodologies to diminish said tumor.

U.S. Patent 4,846,782 discloses a method comprising administering an immunostimulatory dosage (2×10^6 to 5×10^6 IU/m^2) of an α-interferon composition followed by radiation treatment (column 3, lines 4-6 and lines 45-47) that is the same as that claimed.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1, 7, 8 and 15-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Markovic et al[a] (Markovic, S.N. et al., Int. J. Cancer, 45: 788-794, 1990; IDS Ref. "CH") in view of either Golub et al (Golub, S.H. et al., J. Nat. Cancer Inst., 68: 703-710, 1982; IDS Ref. "AO"), Toliou et al. (Toliou, Th. et al, Eur. Urol, 29: 252-256, 1996; IDS Ref. "DH") or Neefe et al. (Neefe, J.R. et al., Cancer Res., 45: 874-878, 1985).

Claim 1 is drawn to a method for treating a human patient with a resectable tumor comprising administering an immunostimulatory dosage of an α-interferon composition. Dependent claim 7 is further limited in that the α-interferon composition is administered for about

5 days prior to resecting the tumor. Claim 8 further limits the subject matter of claim 7 in that the dosage is administered once per day. Claims 15-16 further limit the subject matter of claim 7 in that the α-interferon composition increases T-lymphocyte activation or function. Claim 17 appears to be drawn to the same subject matter as claim 1 because it is not clear how a resectable tumor may be anything other than a solid tumor. Claim 18 further limits claim 17 in the specification of tumor species. Claims 19 and 20 dependent from claim 17 and 18, respectively, further limit the claims in that the tumor is an early stage solid tumor (defined as a tumor that is completely removed by surgery, page 8, lines 31-33). Claims 19 and 20 may be interpreted to read on methods involving tumors that have not detectably metastasized. Claims 21 and 22 are dependent from claim 1 and limit the species of tumor to either renal or melanoma.

Markovic et al[a] teach a method of treating mice with resectable tumors that have not metastasized (Moloney sarcoma virus-induced tumor) comprising administering an α-interferon composition for once a day for 5 days prior to the surgical removal of the tumor (page 789, figure 1). Markovic et al[a] teach dosages in mice that are immunostimulatory and increase the activity and function of cytotoxic T-lymphocytes (page 791).

Markovic et al[a] do not teach a method for human patients or in specific types of cancers. However, it is well known in the art that methods first attempted in animal models may be applied to humans. Golub et al teach that leukocyte interferon (the same as alpha-interferon) increases natural killer cytotoxicity against tumor cell targets in melanoma patients (page 704). Toliou et al teach that interferon α2b administered to patients with renal cell carcinoma, prior to surgery, increases the number of natural killer cells within the tumors and increases the activation and

cytolytic activity of the natural killer cells (abstract and page 253, Table 1). Neefe et al teach that α-interferon increases the immune function of metastatic colon and breast cancer patients (page 877). Thus, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, to have combined the teachings of Markovic et al[a] with either of Golub et al, Toliou et al or Neefe et al to make the invention as claimed. One would have been motivated to combine the teachings of Markovic et al[a] with any of the teachings of Golub, Toliou or Neefe et al because both Markovic et al[a] and either of Golub, Toliou and Neefe demonstrate that the efficacy of interferon-α lies in its ability to stimulate the immune system against a tumor. One would have had a reasonable expectation of success in making the claimed invention because of the teachings by Markovic et al[a] that the mice receiving the interferon-α composition prior to surgery showed a higher prolonged survival and cure than did the control mice.

11. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Markovic et al [b] (Markovic, S.N. et al., Clinical Immunology and Immunopathology, 60: 181-189, 1991; IDS Ref. "CF") in view of either Golub et al (supra), Toliou et al. (supra") or Neefe et al. (supra).

Claim 23 is drawn to a method of preventing post-operative infection comprising administering an immunostimulatory dosage of an α-interferon composition to a human before surgery.

Markovic et al[b] teach that anesthesia inhibits stimulation of natural killer cells in mice by interferon if the interferon is administered after the anesthetic. If the interferon-alpha is administered before the anesthetic then there is no reduction in natural kill cell activity (abstract

and page 185). Markovic et al[b] also teach that anesthesia induced inhibition of natural kill cell stimulation could mean that a surgical patient that is exposed to anesthesia is incapable of activating natural killer defenses in response to pathogenic insults which would lead to an increased susceptibility to post-operative infections (page 187). In view of the teachings of either of Golub et al, Toliou et al and Neefe et al (discussed above) that human patients respond to interferon-alpha administration by increasing natural killer cell activity, the invention of claim 23 is obvious over the prior art. One of ordinary skill in the art would have had a reasonable expectation of success in practicing the invention as claimed by combining the teachings of Markovic et al[b] with the teachings of either of Golub et al, Toliou et al and Neefe et al because of the teachings of Markovic et al[b] that natural killer cells play and active role in the defense against bacterial pathogens (page 181). Thus, the demonstration by Markovic et al[b] that administration of interferon-alpha prior to surgery protects natural killer cells from the inhibitory effects of anesthesia clearly suggests the method of claim 23.

Conclusion

Claims 1, 7, 8 and 13-26 are rejected. Claims 2-6 and 9-12 are objected to for depending from rejected claims. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, Ph.D. can be reached at (703) 308-4310.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

AZH

Anne L. Holleran
Patent Examiner
December 2, 1999

NANCY A. JOHNSON, PH.D
PRIMARY EXAMINER